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FULBRIGHT & JAWORSKI L.L.P.
By Spencer Perkins

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Thierry BOON-FALLEUR et al.
Serial No.	:	08/819,669
Filed	:	March 17, 1997
For	:	TUMOR REJECTION ANTIGEN PRECURSORS, TUMOR REJECTION ANTIGENS AND USES THEREOF
Art Unit	:	1644
Examiner	:	P. Gamble

June 27, 2000

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

DECLARATION

The undersigned hereby declares that, to the best of his knowledge, the information presented in the computer readable form of sequence information submitted herewith is identical to he information presented in the paper copy of sequence information also submitted herewith, and both are identical to information presented in the application as filed. No new matter is believed presented.

Respectfully submitted,
FULBRIGHT & JAWORSKI L.L.P.

By _____
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FULBRIGHT & JAWORSKI L.L.P.
By Veronica Perkins

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DECLARATION

Sir:

The undersigned, being the inventors of subject matter claimed in the above referenced application hereby declare as follows:

1. We have reviewed the office action dated December 27, 1999. We note that, within that office action, the examiner has reviewed the declaration we filed on July 9, 1998, and found it not convincing. We are responding to the examiner's position in this declaration.

2. To begin, the examiner acknowledges that, in the specification of our application, we disclose and discuss a 2.4 kilobase genomic DNA molecule, and a 1.8 kilobase cDNA molecule. The examiner states that the specification does not disclose a 1.7 kilobase cDNA molecule. Presumably, the examiner has raised the point because, in our first declaration, we refer to a 1.7 kilobase cDNA molecule.

3. The 1.8 kilobase cDNA molecule referred to in the specification and the 1.7 kilobase cDNA molecule referred to in our declaration of July 9, 1998, are the same molecule. If example 21 of our specification is reviewed, it will be seen to refer to "an mRNA of about 1.8 kb was identified as homologous, using Northern blot analysis." (Emphasis added). It should be appreciated that determining size via Northern blot analysis is an approximation. One does not sequence a molecule using Northern blotting. When the molecule was sequenced, it was found to contain 1,690 nucleotides, which round off to 1.7 kilobases. Note that in Northern blot work, poly A tails are present. These poly A tails are not considered when giving the length of a cDNA molecule, as these are considered not relevant.

4. The 1.8 kilobase (by Northern blotting) or 1.7 kilobase (by sequencing) cDNA molecule was not the first cDNA molecule we identified. As we reported in our July 9, 1998 declaration, the first cDNA molecule we identified was 1.3 kilobases long. See point "4" of our July 9, 1998 declaration. Given the size of the mRNA, which we had estimated via the Northern blot, we knew that a 1.3 kb cDNA molecule was not complete. We knew that we would have to screen the library again; however, we did begin sequencing work by sequencing the genomic clone (the 2.4 kilobase clone), and our incomplete cDNA clone (the 1.3 kilobase molecule).

5. On May 27, 1991, we sequenced the 1.3 kilobase cDNA molecule. cDNA molecules are double stranded. We sequenced the sense strand of the 1.3 kb cDNA molecule and, over the relevant sequence, we obtained the nucleotides "CCGG." We also prepared bacteria (*E. coli*) which contained the 1.3 kilobase cDNA clone referred to in this paragraph. The bacteria were frozen, and the vials containing these were labeled. Labeling information included the date the frozen material was prepared, a trivial name for the culture, and a description of the insert that had been placed in the *E. coli*. Pierre Vander Bruggen performed this work. He also carried out the initial sequencing of the 1.3kb cDNA clone, referred to above. By reviewing his notebooks, he was able to ascertain that there were still frozen samples of *E. coli* available, which contained copies of the 1.3 kilobase clone he sequenced on May 27.

He has a sample of these bacteria thawed, their viability confirmed, and had the 1.3kb inserts sequenced, on May 8, 2000.

6. We sequenced the genomic clone on June 4, 1991. Genomic DNA is also double stranded. For this molecule, we sequenced the antisense strand, and found an inconsistency with the sequencing we did previously. Specifically, using the antisense sequencing information for the genomic DNA, the sequence over the relevant region was "CGG," i.e., it differed from the 1.3 kilobase region by a "C" nucleotide.

7. As indicated above, we knew that the 1.3 kilobase cDNA molecule was not complete. Hence, we used the 1.3 kilobase cDNA molecule as a probe in the same library we had used when we identified the 1.3 kb cDNA molecule. This time, we identified a molecule (a cDNA clone) which was about 1.7 kb long. This molecule corresponds to that of the mRNA molecule identified as 1.8kb via Northern blotting.

8. The 1.7 kb cDNA molecule was a double stranded molecule. We sequenced the antisense strand of this molecule on July 4, 1991 and it was identical, over the relevant region, to the 2.4 kb gDNA molecule, i.e., the antisense sequencing work led to a sequence of "CGG" over the relevant region. As the 2.4 kb gDNA and 1.8/1.7 kb cDNA molecules were in agreement with each other, we assumed that they provided the correct sequence. As with the 1.3kb cDNA molecule referred to *supra*, Pierre Vander Bruggen carried out this work. Also as with the 1.3kb cDNA molecule, samples of the 1.7kb cDNA molecule were inserted into bacteria, and the bacteria were frozen. The vials which contained the frozen bacteria were labeled, in the same way the frozen bacteria containing the 1.3kb cDNA inserts were labeled. That is, the labels contained information which included the date the frozen material was prepared, a trivial name for the culture, and a description of the insert that had been placed in the *E. coli*. By reviewing his notebooks, Pierre Vander Bruggen was able to ascertain that there were still frozen samples of *E. coli* available which contained copies of the 1.7kb cDNA clone he had sequenced on July 4, 1991. He had a sample of these bacteria thawed, their viability confirmed, and had the 1.7kb cDNA inserts sequenced, on April 25, 2000.

9. In the case of both the 1.7kb cDNA molecule and the 1.3kb cDNA molecule, Pierre Vander Bruggen had both strands of the molecule sequenced (as indicated, on April 25, 2000, and May 8, 2000, respectively).

10. Pierre Vander Bruggen then compared the sequences of the 1.3kb and 1.7kb cDNA molecules to each other, to the corrected sequence submitted previously and to the originally filed sequences. The sequence information of April 25 and May 8, 2000, indicated that, indeed, the sequences presented in the application as filed originally contained an error, in that there was a "C" missing, as reported in prior declarations.

11. It is our position that we can state this with absolute certainty because the cDNA inserts which Pierre Vander Bruggen had sequenced on April 25 and May 8 were frozen samples of the same clones that he had sequenced on July 4, 1991, and May 27, 1991.

12. We have explained, previously why we believe the original error occurred. We remain of this view.

13. We hereby declare that all statements made herein of our own knowledge are true and that the statements made on information and belief, are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

_____ _____

Thierry Boon Falleur Date

_____ _____

Pierre Vander Bruggen Date

_____ _____

Benoit van den Eynde Date

Aline Van Pel	Date
Etienne De Plaen	Date
Christophe Lurquin	Date
Patrick Chomey	Date
Catia Traversari	Date